

REMARKS

The Examiner has rejected claims 15-16 under 35 U.S.C. § 103(a) as being unpatentable over Spinella et al (1994) (“Spinella”), in view of Wei et al (1994) (“Wei”) and U.S. Patent No. 6,017,699 to Jordan (“Jordan”). Claims 15-16 are currently pending. The following remarks are considered by applicant to overcome each of the Examiner's outstanding rejections to current claims 15-16. An early Notice of Allowance is therefore requested.

I. SUMMARY OF RELEVANT LAW

The determination of obviousness rests on whether the claimed invention as a whole would have been obvious to a person of ordinary skill in the art at the time the invention was made. In determining obviousness, four factors should be weighed: (1) the scope and content of the prior art, (2) the differences between the art and the claims at issue, (3) the level of ordinary skill in the art, and (4) whatever objective evidence may be present. Obviousness may not be established using hindsight or in view of the teachings or suggestions of the inventor. The Examiner carries the burden under 35 U.S.C. § 103 to establish a *prima facie* case of obviousness and must show that the references relied on teach or suggest all of the limitations of the claims.

II. REJECTION OF CLAIMS 15-16 UNDER 35 U.S.C. § 103(A) BASED ON SPINELLA, IN VIEW OF WEI AND JORDAN

In paragraph 3 of the current Office Action, the Examiner rejects claims 15-16 under 35 U.S.C. § 103(a) as being unpatentable over Spinella, in view of Wei and Jordan. This rejection is respectfully traversed and believed overcome in view of the following discussion.

With respect to this rejection, Examiner contends that the combination of references discloses all of the limitations of independent Claim 15, including “SEQ ID Nos:

33-55". Office Action (7/13/06), P. 3 (citing Spinella, P. 114-115, Fig. 9.3). However, this assertion misconstrues the teachings of Spinella. Namely, as is described in detail below, the disclosure in Spinella of "the 24 known TCR V_β families" does not disclose "SEQ ID Nos: 33-55".

Independent Claim 15 states, in part:

"A kit for assessing the expression of T cell receptor variable subunit β in a patient, said kit comprising **SEQ ID Nos: 33-55....**" (emphasis added)

SEQ ID Nos: 33-55 are defined in Table 2 of the current application as:

TABLE 2

TCRVa family	Sequence	SEQ ID No:	Ref.
B1	CCGCACAAACAGTTCCCTGACTTGC	33	†
B2	GGCCACATACGAGCAAGGCGTC	34	‡
B3	CGCTTCTCCGGATTCTGGAGTCC	35	†

TABLE 2-continued

TCRV α family	Sequence	SEQ ID NO:	Ref.
B4	TTCCCATCAGCCGCCAAACCTAA	36	†
B5	TGTGTCCTGGTACCAACAG	37	
B6	CAGCGCACAGAGCAGGGG	38	
B7	CCTGAATGCCCAACAGCTCTC	39	
B8	GGTACAGACAGACCATGATGC	40	
B9	TTCCCTGGAGCTTGGTGAECTCTGC	41	†
B11	TGCCAGGCCCTCACATACTCTCA	42	†
B12.1	TGTCACCACTGAGAACCAACC	43	
B13.1	CTGCAGTGTGCCAGGATATGAACC	44	
B14	GAGTCGCCAGCCCCAAC	45	
B15	CAGGCACAGGCTAAATTCTCCCTG	46	†
B16	GCCTGCAGAACTGGAGGATTCTGG	47	†
B17	GAAAGGAGATATAGCTGAAGGGTAC	48	‡
B18	GATGAGTCAGGAATGCCAAAGG	49	
B20	CTGGCTTCTATCTCTGTGCCTGG	50	
B21	CCACTCTCAAGATCCAGCCTGC	51	
B22	AAGTGATCTTGCCTGTGTCCCCA	52	†
B23	CAGGGTCCAGGTCAGGAC	53	
B24	CCCAGTTGGAAAGCCAGTGACCC	54	†
B25	GAAACAGGTATGCCAAGGAAAG	55	

† These primers were defined in Genevee-Gaudin, et al., Eur. J. Immunol. 1992 22:1261-1269;

‡ These primers were defined in Blumberg, et al., J. Immunol. 1993 150 (11):5144-5153.

The listings for which no reference is entered have been uniquely identified as recognizing every member of that TCRV family.

However, Spinella only states that their "approach to the problem has been to employ a standard reference template in the PCR that consists of cloned TCR genes corresponding to each of the 24 known TCR V_β families." Spinella, P. 114. Later on, Spinella discloses TCR β family specific oligonucleotide primers in Table 9.1:

TABLE 9.1. TCR β family-specific oligonucleotide primers and their amplification efficiencies when paired with the C_βa antisense primers.*

Family	Sequence
C _β RT	GCGGCTGCTCAGGCAGT
C _β a	CAGGCAGTATCTGGAGTCATTGA
C _β s	GTGTTCCCACCCGAGGTCGC
V _β 1	AAGAGAGAGCAAAAGGAAACATTCCTT
V _β 2	TCAGGCCACAACATATGTTTGTT
V _β 3	GTCTCTAGAGAGAAGAAGGAGC
V _β 4	ACAGAGCCTGACACTGATCGC
V _β 5	CTGATCAAACGAGAGGACAGCA
V _β 6	CTCAGGTGTGATCCAATTTC
V _β 7	GGAATGACAATAAGAAGTCTTG
V _β 8	TTTACTTTAACAAACACGTTCCGA
V _β 9	GAACAAAAACTGGGCCATGATACT
V _β 10	GGATTGTGTTCTATAAAAAGCACA
V _β 11	GTTCTCAAACCATGGGCCATGA
V _β 12	CACCAGACTGAGAACCAACC
V _β 13	TGTGCCAGGATATGAACCAT
V _β 14	CAGAACCCAAGATAACCTCATCAC
V _β 15	CTGGAATGTTCTCAGACTAAGGGT
V _β 16	AAAGAGTCTAACAGGATGAOTCC
V _β 17	GAACAGAATTGAAACCACGATGCC
V _β 18	GCAGCCCCATGAAAGGACACAG
V _β 19	CAAAGATGGATTGTACCCCCGAA
V _β 20	TGTGGAGGGAACATCAAACCCC
V _β 21	GATTACAGTTGCCCTAAGGA
V _β 22	AAAGAGGAAACAGCCACTCTG
V _β 23	CTGTGTCCCCATCTTAATCAC
V _β 24	GTGACCCCTGAGTTGTTCTCAGA

*The C_βa sense primer is used together with C_βa to amplify the C_β region in a separate PCR reaction. The C_β RT primer is used to reverse transcribe from total RNA prior to PCR amplification.

None of the TCR β family specific oligonucleotide primers in Table 9.1 of Spinella disclose SEQ ID Nos: 33-55 as stated in Claim 15.

In addition, neither does a general disclosure of "cloned TCR genes corresponding to each of the 24 known TCR V_β families" disclose SEQ ID Nos: 33-55 as stated in Claim 15. Such a disclosure is too general and discloses only the families generally, and not the specific SEQ ID Nos: 33-55 as stated in Claim 15. This is illustrated by Wei, to

which Examiner cites in support of the disclosure of the TCR β 55 gene. Office Action (7/13/06), P. 2-3. Wei discloses a nucleotide sequence of the BV25S1 gene. Wei, P. 202, Fig. 1. This gene is over nine hundred sixty nucleotides long. The longest sequence of any of SEQ ID Nos: 33-55, as stated in Claim 15, is only twenty-five nucleotides long. "Within a gene, the sequence of nucleotides along a DNA strand defines a messenger RNA sequence which then defines a protein, that an organism is liable to manufacture or 'express' at one or several points in its life using the information of the sequence." Wikipedia, <http://en.wikipedia.org/wiki/DNA> (obtained from the web page on 10/3/06). As such, if you change the sequence of nucleotides, you can change the RNA sequence defined by that changed sequence, which in turn would change the protein defined by that changed RNA sequence. Accordingly, a sequence of over nine hundred sixty nucleotides is not the same as a sequence of twenty-five nucleotides. As such, the combination of Spinella and Wei fail to disclose SEQ ID Nos: 33-55 as set forth in Claim 15.

As such, Applicants respectfully assert that Examiner has failed to establish a *prima facie* case of obviousness of independent Claim 15 and corresponding Claim 16 because it is dependent from Claim 15. Therefore, Applicants respectfully request that Examiner remove the rejection of claims 15-16 under 35 U.S.C. § 103(a) as being unpatentable over Spinella et al (1994), in view of Wei et al (1994) and U.S. Patent No. 6,017,699 to Jordan.

Based upon the above remarks, Applicants respectfully request reconsideration of this application and its early allowance. Should the Examiner feel that a telephone conference with Applicants' attorney would expedite the prosecution of this application, the Examiner is urged to contact him at the number indicated below.

Respectfully submitted,

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